Surgery for Acquired Cardiovascular Disease

Reverse remodeling and improved regional function after repair of left ventricular aneurysm

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Background: Changes in regional left ventricular mechanics after anteroapical aneurysm repair in human subjects can be studied noninvasively by means of magnetic resonance tagging. We hypothesized that left ventricular intramyocardial function would improve throughout the left ventricle after repair.

Methods: We studied 6 male patients with a left ventricular anteroapical aneurysm (mean age ± SD, 63 ± 5 years) using magnetic resonance tagging 3 ± 1 weeks before and 6 ± 1 weeks after aneurysm repair, coronary artery bypass grafting, and mitral valve repair (n = 2). Breath-hold tagged imaging spanned the left ventricle in the short axis from apex to base. Left ventricular mass, end-diastolic and end-systolic volume, and ejection fraction were measured. Two-dimensional strain analysis was applied; averaged for the apical, middle, and basal left ventricle and the whole left ventricle; and expressed as greatest lengthening (similar to wall thickening), greatest shortening, and angular deviation of the lengthening strain from the radial direction.

Results: After aneurysm repair, left ventricular mass decreased from 373 ± 27 to 333 ± 25 g ($P < .05$), end-diastolic volume from 212 ± 22 to 168 ± 18 mL ($P < .005$), and end-systolic volume from 188 ± 26 to 113 ± 18 mL ($P < .005$); ejection fraction improved from 13% ± 4% to 23% ± 4% ($P < .005$). For the whole left ventricle, lengthening strain increased from before to after the operation (8% ± 1% to 10% ± 1%, $P < .01$). Most of the improved lengthening occurred at the middle left ventricle (8% ± 1% to 11% ± 1%, $P < .01$), in the base (8% ± 1% to 10% ± 1%, $P < .05$), and in the inferior wall (9% ± 1% to 12% ± 1%, $P < .05$). Lengthening tended to become more radially oriented, decreasing from 31° ± 3° to 27° ± 3° ($P = .10$). Shortening strain did not change (10% ± 1% to 11% ± 1%, P = not significant).

Conclusions: Left ventricular aneurysm repair is associated with reverse remodeling and an improvement in the extent and orientation of intramyocardial function, especially at the middle and basal left ventricle and inferior wall.

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New surgical approaches to the management of patients with severely depressed left ventricular (LV) systolic function and chronic coronary artery disease are now available.[1] Treatment of LV aneurysm by repair is one such therapy.[2] Two different approaches are presently used: (1) linear LV aneurysm excision and repair[3] and (2) patch repair with septal exclusion, such as that advanced by Dor and colleagues.[4] Because of limitations in the imaging techniques used, analysis of myocardial function in previous clinical studies has been limited to changes in global LV size and function[2,5-7] and LV shape.[8] Changes in LV intramyocardial systolic performance are therefore incompletely understood.

Magnetic resonance (MR) myocardial tagging is a noninvasive method for evaluating regional intramyocardial function[9,10] in patients with cardiac disease[11,12] and can be used to evaluate 2-dimensional intramyocardial strains in healthy subjects[13] and patients.[14] We have used MR tagging to define the improvements in intramyocardial function that occur with the reverse remodeling associated with aneurysm resection and repair.

Methods

Six male patients with coronary artery disease and previous anterior infarction with known LV anteroapical aneurysms were entered into the study. Patient characteristics are listed in Table 1. The Allegheny General Hospital Institutional Review Board approved the study in accordance with institutional guidelines, and all subjects provided informed consent. The patients underwent magnetic resonance imaging (MRI) 3 ± 1 weeks before the operation and again 6 ± 1 weeks after the operation.

Nine normal human volunteers with no historical or echocardiographic evidence of heart disease (mean ± SD age, 32 ± 4 years) were also studied.

The MRI was performed in a Siemens 1.5T Vision scanner (Siemens Corporation, Erlanger, Germany) with the patient supine and with a 4-element, phased-array body coil around the chest. After scout imaging to localize the LV short axis, breath-hold gradient echo cine MR tagging was performed, with multiple 7-mm thick short-axis slices covering the heart from apex to base (Figure 1).[12] The repetition time was 35 or 45 ms with view sharing, and the echo time was 4 ms, yielding a temporal resolution of 35 to 45 ms. The field of view was 300 mm, with a matrix size of 128 × 256, interpolated to 256 × 256 for display, yielding an effective resolution of 1.17 × 1.17 mm. Each set of images was obtained during a 15- to 18-heartbeat breath hold. In addition, untagged cine MRI was performed in 2-chamber and 4-chamber long-axis planes with similar image parameters as above, except with a 40- to 50-ms temporal resolution between frames (Figure 2).

In accepting patients for surgical intervention, the definition of an aneurysm was broadly applied. Rather than limiting it to patients with a well-defined scar, saccular appearance, defined neck, and dyskinesia, we included patients with akinetic scars that contributed to global ventricular enlargement. The operative procedure was performed with conventional cardiopulmonary bypass techniques. Concurrent procedures included coronary artery bypass in all 6 patients and mitral valve repair in 2 patients. Two of the 6 patients had single-vessel left anterior descending artery disease, 2 had 2-vessel disease, and 2 had 3-vessel disease. All hearts were protected with cold-blood cardioplegic solution administered both antegradely and retrogradely. The aneurysm repair was performed with the heart arrested. The sequence of procedures (when performed) was distal coronary anastomosis, mitral valve repair, aneurysm repair, and proximal coronary anastomosis. All patients had a linear repair with septal exclusion. Horizontal mattress sutures of 0 Prolene polypropylene (Ethicon, Inc, Somerville, NJ) were brought through a Teflon felt strip and then through the LV free wall across the ventricular cavity to the base of the scar in the midseptum, up and out through the top of the septum medially or laterally to the left anterior descending artery, and then through a Teflon felt strip. Once these were tied, the felt strips and edges of the scar were reinforced with a double-layer 3-0 Prolene baseball stitch for strain relief. Every attempt was made to completely exclude the infarcted portion of the septum. LV mass, end-dia-

TABLE 1. Clinical characteristics of the study population

Patient no.	Age (y)	Sex	Surgical technique	CABG	MV repair	Medications
1	60	M	LV aneurysm resection, linear repair	LITA, SVG × 3	Yes, Cosgrove 26 ring	Coumadin, enalapril, digoxin, lasix, amiodarone
2	77	M	LV aneurysm resection, linear repair	SVG × 3	No	ASA, lasix, atenolol, digoxin, accupril
3	64	M	LV aneurysm resection, linear repair	SVG ×1	Yes, Cosgrove 28 ring	ASA, coumadin, digoxin, hydralazine, lasix
4	64	M	LV aneurysm resection, linear repair	LITA, SVG ×1	No	ASA, lopressor, lescol
5	42	M	LV aneurysm resection, linear repair	LITA, SVG ×1	No	Carvedilol, demedex
6	73	M	LV aneurysm resection, linear repair	SVG ×1	No	ASA, digoxin, Imdur, lopressor, lasix

CABG, Coronary artery bypass grafting; *MV*, mitral valve; *LITA*, left internal thoracic artery; *SVG*, saphenous vein graft; *ASA*, aspirin.

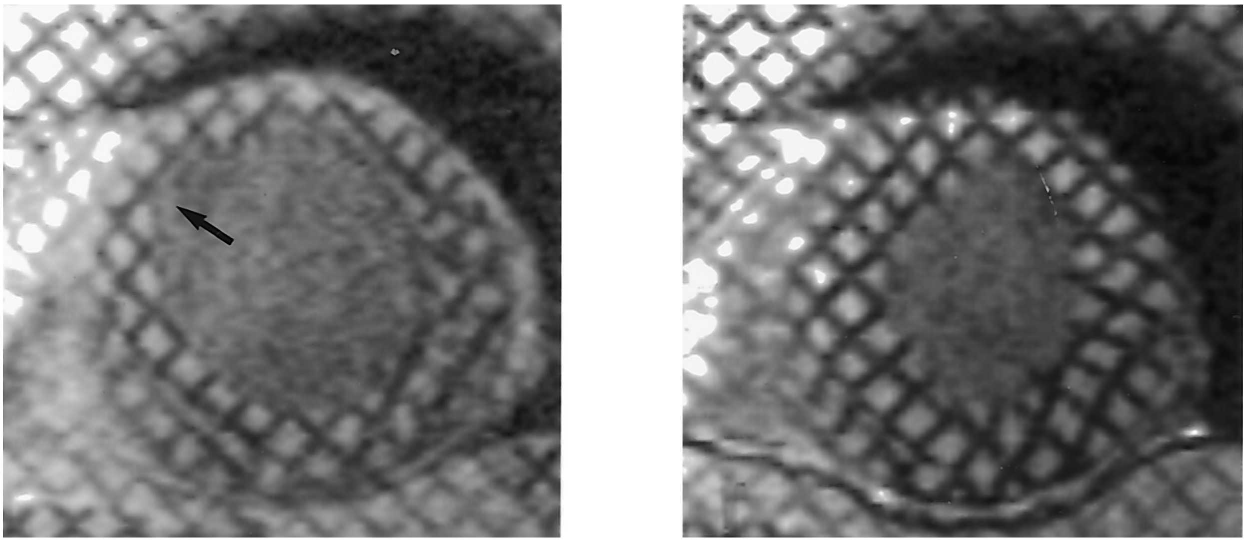

Figure 1. End-systolic apical short-axis MR tagged images in the same patient before *(left)* and after *(right)* LV aneurysm repair. The tag stripes are the dark lines embedded noninvasively in the myocardium in a grid pattern at end-diastole that in normal tissue will deform such that squares at end-diastole become trapezoids at end-systole, with more shortening toward the endocardium. The thinning of the anteroseptum *(arrow)* can be appreciated before the operation. After the operation, the cavity area in this slice is reduced, the wall thickness of the anteroseptum is improved, and deformation of the tag stripes is mildly improved.

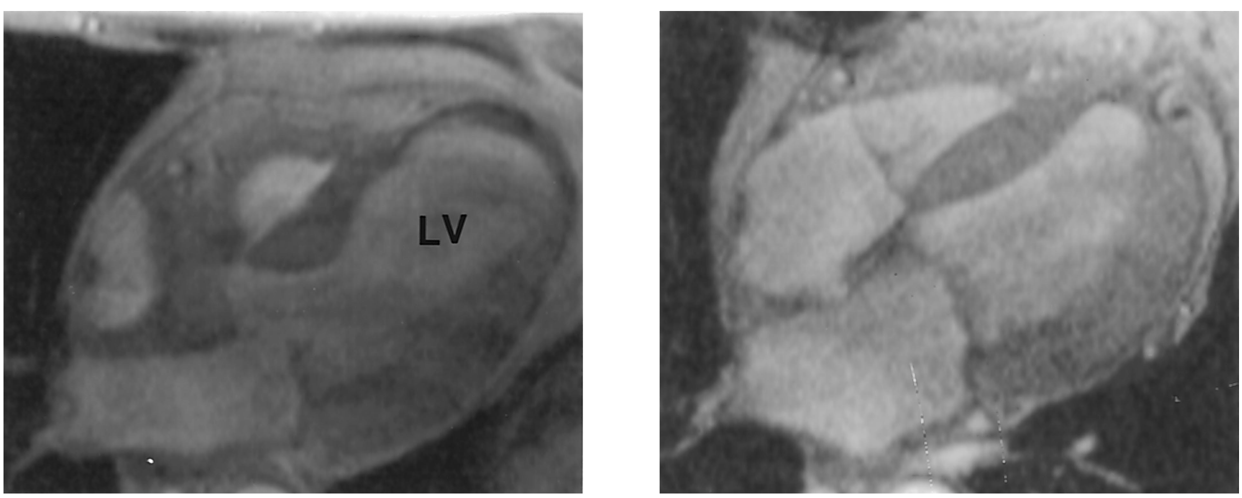

Figure 2. End-systolic, 4-chamber, long-axis cine MRI in the same patient as in Figure 1 before *(left)* and after *(right)* LV aneurysm repair, with the left ventricle *(LV)* as marked. The thinned apex can be readily seen before the operation in the left image. At right, the thinned region makes up much less of the apex, and the overall LV geometry is improved, with a reduction in end-systolic cavity area compared with that before the operation.

stolic and end-systolic volumes, and ejection fraction were calculated from planimetered epicardial and endocardial areas at end-diastole and end-systole from short-axis images by a trained operator using a personal comupter and Siemens ImageView software (Siemens Corporate Research, Iselin, NJ) and applying previously published techniques.[15] Two-dimensional strain analysis was performed on all short-axis slices with the SPAMMVU software (University of Pennsylvania) on a SiliconGraphics Indigo workstation (SiliconGraphics Computer Systems, Mountain View, Calif) by a trained image analyst using previously published techniques (Figure 3).[13,14] L1 was defined as the greatest systolic lengthening or wall thickening in normal subjects (Figure 3). L2 was defined as the greatest systolic shortening, which is in the circumferential direction in healthy patients. β Values were defined as the angular deviation of L1 from the radial direction (Figure 3), which is approximately 10° in normal subjects.[13,14]

For the analysis of regional function, LV regions were averaged by means of short-axis and long-axis location and for the entire left ventricle. Results in patients for LV structure and function were compared before and after the operation by using the paired Student *t* test. Results between patients and normal subjects were compared by using the unpaired Student *t* test. All results are expressed as means ± SE.

Results

Representative 4-chamber, long-axis cine images from a patient before and after aneurysm repair are shown in Figure 2. LV mass was 373 ± 27 g before the operation in the patient group and decreased to 333 ± 25 g after the operation ($P < .05$). LV end-diastolic volume decreased from 212 ± 22 to 168 ± 18 mL ($P < .005$), and LV end-systolic volume decreased from 188 ± 26 to 113 ± 18 mL ($P < .005$). Therefore, LV ejection fraction rose from 13% ± 4% preoperatively to 23% ± 4% postoperatively ($P < .005$).

The analysis of 2-dimensional strains averaged for the entire left ventricle are shown in Figure 4. In normal subjects L1 is 16% ± 1%, L2 is 21% ± 1%, and β is 12° ± 1°. Before the operation, patient L1 was 8% ± 1% ($P < .001$ vs normal levels) and improved to 10% ± 1% after the operation ($P < .01$) but not back to normal levels. L2 was similarly reduced before the operation to 10% ± 1% ($P < .001$ vs normal levels) but did not improve after the operation (11% ± 1%, P = not significant). β Values were significantly increased in patients compared with those in normal subjects (31° ± 3° vs 12° ± 1°, $P < .001$) and tended to decrease, although not significantly, after the operation (to 27° ± 3°, $P = .10$).

Regional data along the long axis of the left ventricle from the patients before and after the operation are presented in Table 2. The improvement in L1 after the operation was due to improvements in the maximal lengthening at the middle left ventricle and base. The middle left ventricle improved from 8% ± 1% to 11% ± 1% ($P < .06$), and the base improved from 8% ± 1% to 10% ± 1% ($P < .01$). There was no regional improvement in L2 or β, although β at the middle left ventricle tended to decrease (from 32° ± 7° to 23° ± 14°, $P = .15$).

Regional data along the short axis of the left ventricle from the patients before and after the operation are presented in Table 3. The improvement in L1 after the operation was mostly due to improvement in function in the inferior wall. The inferior wall improved from 9% ± 1% to 12% ± 1% ($P < .05$). L1 tended to improve in the septum from 8% ± 1% to 10% ± 1% ($P = .10$). There was no regional improvement in L2 or β, although β also tended to decrease in the inferior wall (from 23° ± 4° to 17° ± 2°, $P = .07$).

Discussion

LV aneurysm repair in this patient population with severe ischemic LV systolic dysfunction was associated with reverse remodeling. LV end-diastolic and end-systolic volumes decreased significantly, and LV mass likewise decreased, as might be expected. LV ejection fraction improved globally. Regional LV mechanics improved to some extent in these remodeled ventricles. Intramyocardial lengthening improved in extent and tended to improve in orientation (became more radially directed). These improvements were most marked at the middle left ventricle and at the base and in the inferior wall, remote from the aneurysm. To the best of our knowledge, this study represents

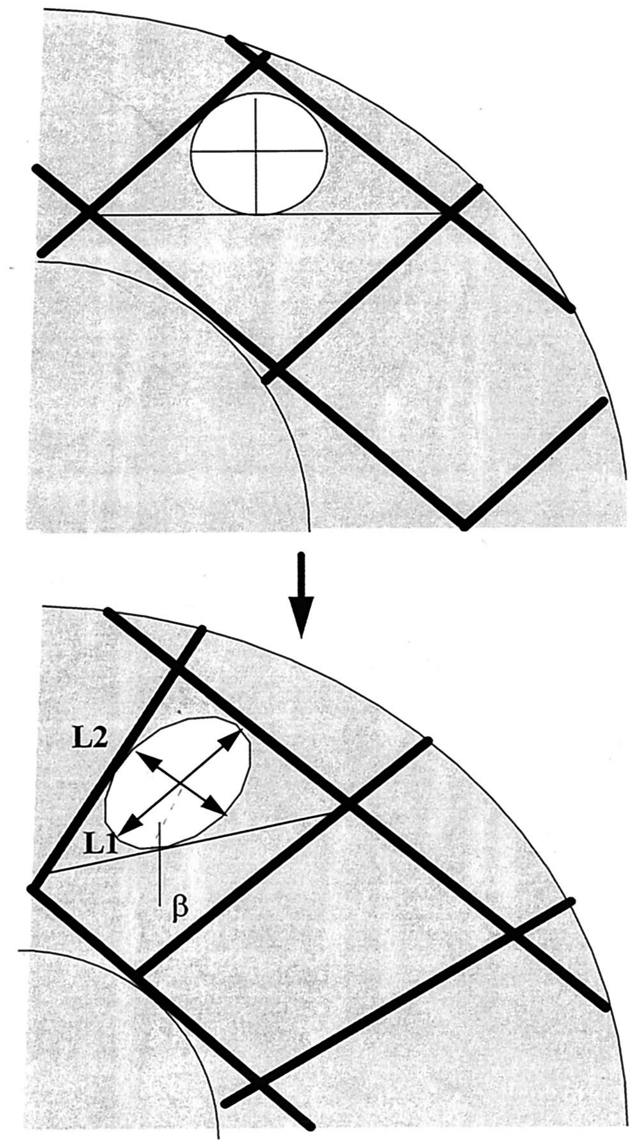

Figure 3. Schematic representation of the strain analysis at end-diastole and end-systole in a single triangle defined by tag-stripe intersections within the wall of the left ventricle in the short axis (one fourth of the LV wall circumference is represented). The triangle has deformed at end-systole. *L1*, Greatest systolic lengthening; *L2*, greatest systolic shortening; β, angular deviation of L1 from the radial direction.

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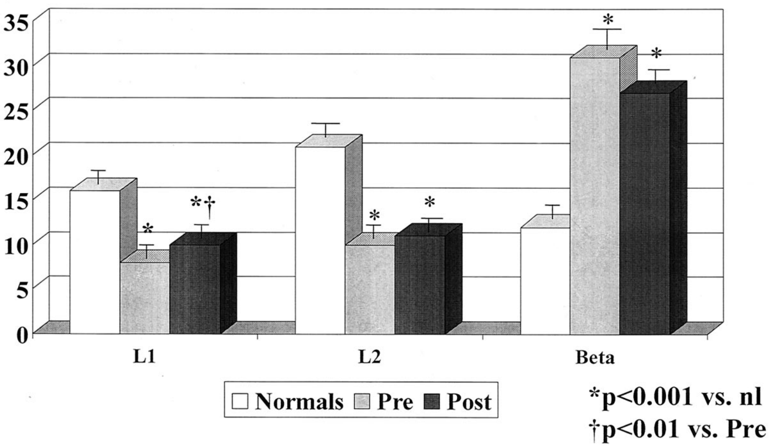

Figure 4. Graphic representation of L1 (greatest lengthening), L2 (greatest shortening), and β (angular deviation of L1 from the radial direction) in normal subjects *(open bars)* and in patients before the operation *(shaded bars)* and after the operation *(filled bars)*. The y axis is in percentages for L1 and L2 and in degrees for β. *$P < .001$ versus normal subjects; †$P < .01$ versus values before the operation.

TABLE 2. Regional 2-dimensional strain data of patients before and after the operation by location along the long axis of the left ventricle

		Before the operation	After the operation	*P* value
	Apex	8% ± 1%	8% ± 1%	NS
L1	Mid	8% ± 1%	11% ± 1%	<.06
	Base	8% ± 1%	10% ± 1%	<.01
	Apex	9% ± 1%	11% ± 1%	NS
L2	Mid	10% ± 2%	10% ± 1%	NS
	Base	11% ± 1%	10% ± 1%	NS
	Apex	37° ± 4°	37° ± 7°	NS
β	Mid	32° ± 7°	23° ± 4°	NS
	Base	23° ± 2°	20° ± 2°	NS

NS, Not significant.

TABLE 3. Regional 2-dimensional strain data of patients before and after the operation by location along the short axis of the left ventricle

		Before the operation	After the operation	*P* value
	Anterior	7% ± 1%	7% ± 1%	NS
	Lateral	8% ± 1%	9% ± 1%	NS
L1	Inferior	9% ± 1%	12% ± 1%	<.05
	Septum	8% ± 1%	10% ± 1%	.10
	Anterior	8% ± 1%	9% ± 1%	NS
	Lateral	10% ± 1%	9% ± 1%	NS
L2	Inferior	13% ± 1%	13% ± 1%	NS
	Septum	10% ± 1%	11% ± 1%	NS
	Anterior	43° ± 7°	38° ± 10°	NS
β	Lateral	28° ± 2°	28° ± 5°	NS
	Inferior	23° ± 4°	17° ± 2°	.07
	Septum	29° ± 5°	25° ± 5°	NS

NS, Not significant.

the first to directly measure changes in intramyocardial function noninvasively before and after aneurysm resection.

Previous studies in an ovine model of LV anteroapical aneursym have suggested mechanical effects of the aneurysm on noninfarcted regions caused by elevated local wall stress.[15] At 6 months after myocardial infarction, intramyocardial function remains depressed in noninfarcted regions adjacent to the aneurysm.[15] In the same model stiffness of the aneurysm has been shown to increase at 1 week after myocardial infarction but then to gradually decrease to preinfarction levels by more chronic stages (6 weeks) after myocardial infarction.[16] These authors suggested that this increase in compliance leads to increased wall stress and decreased mechanical performance globally. The beneficial effects of aneurysm resection on regional mechanical performance in the present study may be due to reductions in local wall stress in remote regions.

Aneurysm plication in the same ovine model causes an immediate decrease in LV volume and diastolic compliance.[17] Plication increases end-systolic elastance[17,18] and the relationship between stroke work and end-diastolic volume,[17] likely because of reduced diastolic stretching of border myocardium and reducing wall stresses in border and remote myocardium.[18] However, 6 weeks later, all of these values return to preplication levels.[17] Interestingly, maximal principal strain and its orientation were improved in the present study at 6 weeks after the operation, suggesting that in human subjects there may be persistence of the benefits of aneurysm plication on myocardial performance.

Finite element analysis demonstrates that end-systolic elastance and preload recruitable stroke work can improve with anteroapical aneurysm resection in the human left ventricle.[19] However, diastolic compliance also increases, resulting in a small decrease in the Starling relationship. A similar analysis with a multiple-compartment elastance model suggested that overall pump function (the Starling relationship) was depressed but that, because of wall-stress reductions, overall cardiac efficiency would improve, leading to long-term benefits[20] that were indeed seen in our patients.

Previous studies using left ventriculography have documented improvements in regional function after aneurysm repair.[5] Of 69 patients in 1 series, 25 were studied both preoperatively and postoperatively. LV ejection fraction improved from 31% $\pm$ 12% to 43% $\pm$ 13% postoperatively. Seventeen patients showed improved LV regional function, mostly increased wall thickening in the remote inferior wall. The only predictor of functional improvement postoperatively was an abnormal regional curvature at the inferior aneurysm border.[5,21] No difference in outcome has been seen on the basis of whether the aneurysm is akinetic or dyskinetic before resection.[22]

Our study group is small. However, the number of measurements allowed by MR tagging throughout the left ventricle make it a very powerful method for quantitating intramyocardial function. The effects on myocardial function of an adjoining akinetic or dyskinetic scar are minimized because the analysis by MR tagging measures active, as opposed to passive, motion.

All of the patients underwent a linear repair rather than patch repair. The results may not be applicable to the latter procedure, although we did exclude the septal infarct, a differentiating characteristic of patch repair from classic linear repair. Two of the patients underwent concomitant mitral valve repair. A previous study by our group[23] has demonstrated that mitral valve repair in patients with severe mitral regurgitation is associated with improvement in L1, and this may account for some of the improvement in those patients. However, the angle, β, did not improve after mitral valve repair.

The analysis performed was a 2-dimensional analysis in the short-axis planes, and the full 3-dimensional capabilities of MRI were not used. Three-dimensional analysis of tagged MR images may improve the understanding of ventricular mechanics by imparting information on 3-dimensional strains.[13] However, because of time constraints and the severity of the patients' underlying heart failure preoperatively, long-axis imaging was not performed in every patient. Because of the nature of the 2-dimensional analysis performed and the tag stripe spacing with triangles defined by tag stripe intersections, most of the measurements are made in the midwall. The method therefore does not allow differentiation of subendocardial from subepicardial 2-dimensional strains, which may vary by region in the left ventricle, as previously demonstrated in animals and human subjects.[24,25] This can be examined in a 1-dimensional strain analysis of tagged data, but one would then lose the important information regarding the angle of deformation.

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